أفضل ما نبتدي به هو حمد الله عز وجل بما هو أهله،ثم الصلاة على محمد عبده و رسوله خاصة ، وجميع أنبيائه عامة.

أما بعد،

أتمنى لكم جميعا – إخواني و أخواتي – التوفيق في آخر امتحان لنا في هذا العام وبعد ساعات من الآن سوف نقبل على إجازتنا الصيفية أهديكم بهذه المناسبة، أبيات للشاعر القدير إليا أبو ماضي قالها في الصيف:

ما أحلى الصيف ما أكرمه ملأ الدنـــــيا رخاء و رفاها
عندما رد إلى الأرض الصبى رد أحلامي التي الدهر طواها
كنت أشكو مثلما تشكو الضنى فشفى ألام نفسي و شـــفاها

فأسأل الله لكم جميعا التوفيق و السداد، و أتمنى لكم إجازة سعيدة، و نراكم في العام المقبل إن شاء الله.

Ahmed Al-Aqeel **Bio team leader**

Thanx for
Dr.Abo yosra

Bio girlz team
(Angel eyes – bush bush –Nova – Noora)
Thnx Dr.nour

أحبائي في هذه المذكرة حاولنا أن نجمع كل معلومة مهمة ...

هذا الباب يعادل نصف الفاينل يعني ١٥ درجة باذن الله هي من نصيب الجميع ،،

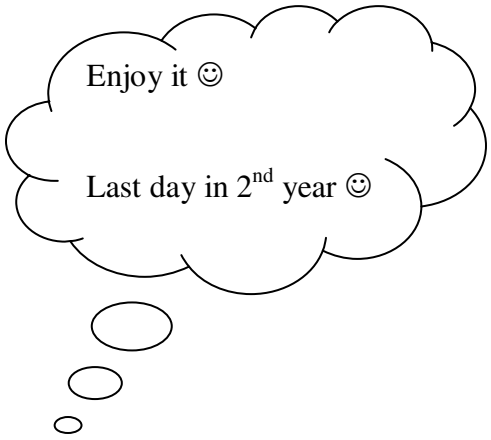
في باب البلود نزلت مذكرتين قبل هذه المذكرة ...

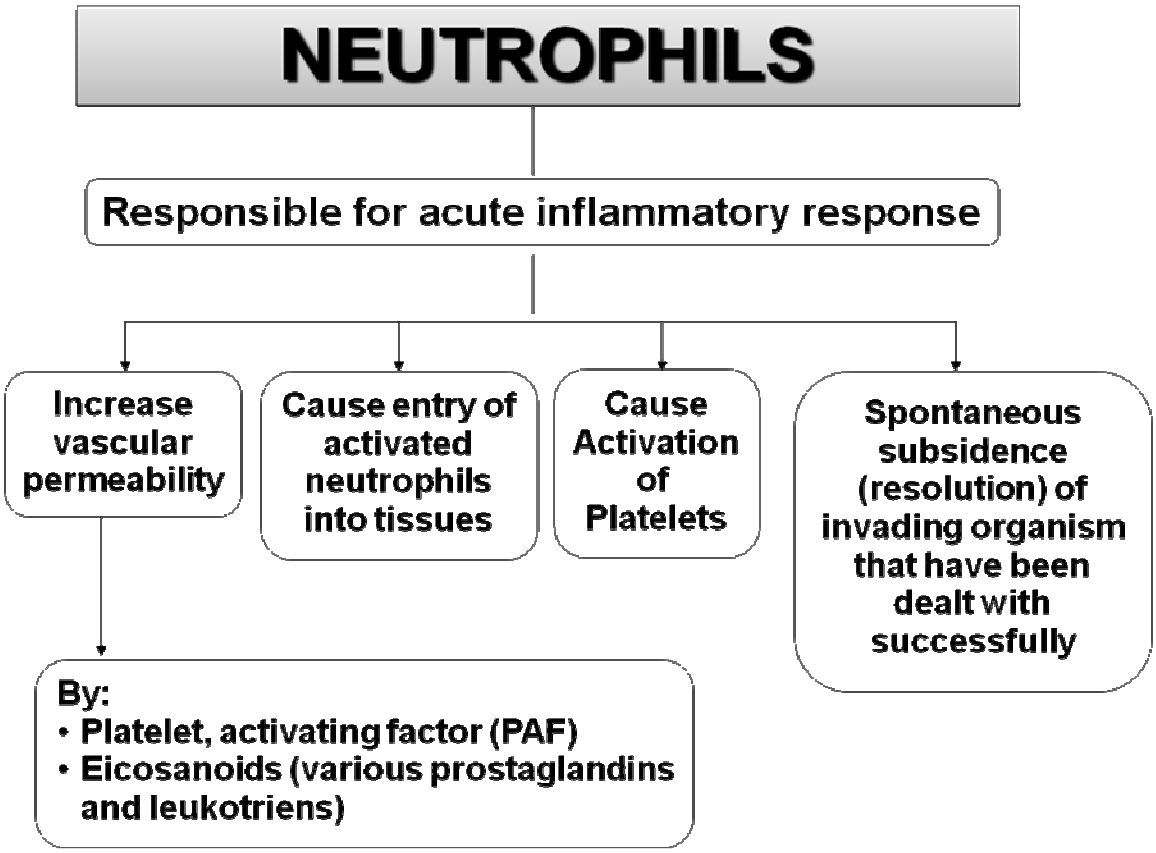
بالاضافة الى الباب الثالث بالكتاب مطلوبة كاملة ...

بالنسبة لما يتعلق بهذه المذكرة فهي عبارة عن محاضرات الطلاب والطالبات مجتمعة ...

لكم مني أطيب تحية

أحمد العقيل





FUNCTIONS OF MONOCYTES:

- Monocytes are precursors of macrophages, which are actively involved in phagocytosis.

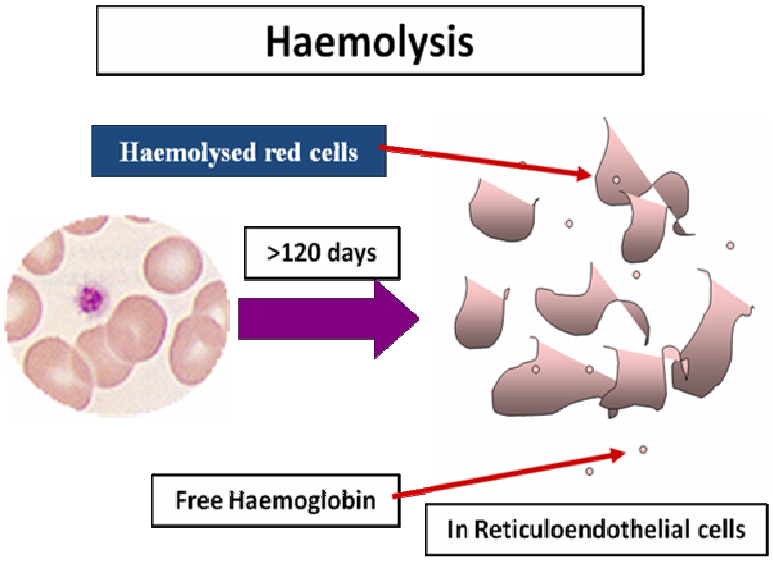
FUNCTIONS OF LYMPHOCYTES:

- **B-Lymphocytes:**
  - Synthesize and secrete antibodies (humoral immunity)
- **T-Lymphocytes:**
  - Involved in cellular immune mechanism e.g
    - ✓ killing virally infected cells and some cancer cells.
    - ✓ activate B cells to make antibodies.

PLATELETS

- Involved in coagulation of blood

Haemolysis of Erythrocytes

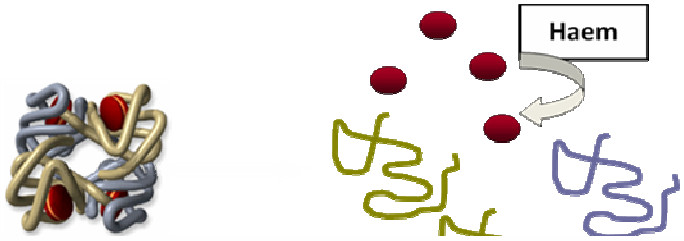


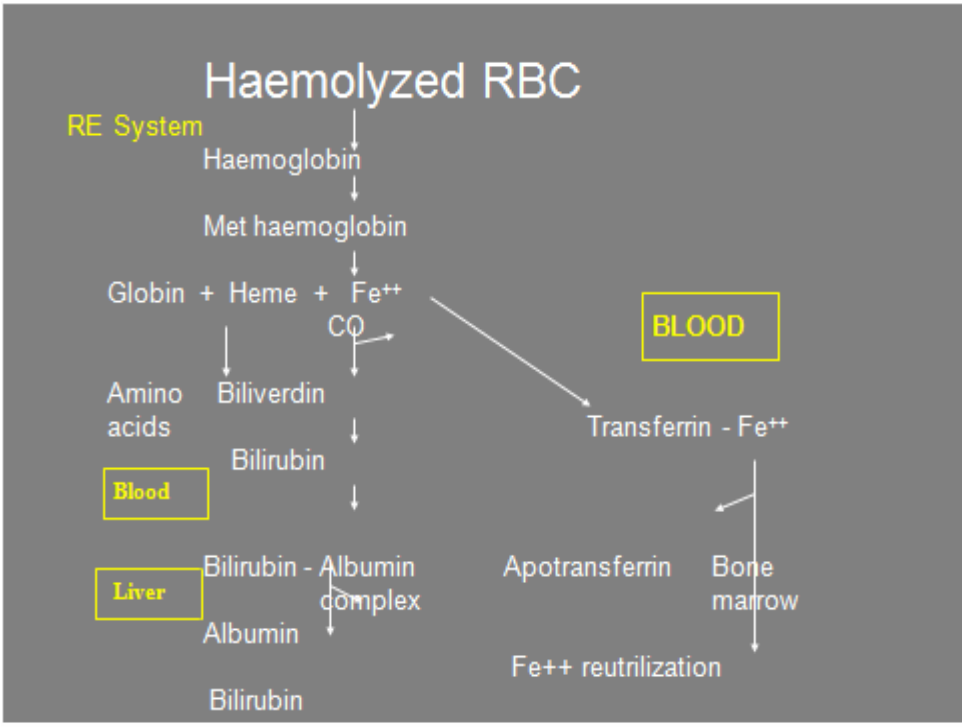
Haemolysis of Erythocytes :

- After a life span of 120 days, erythrocytes are haemolysed
- **In:**
  - Spleen
  - Bone marrow
  - Other REC

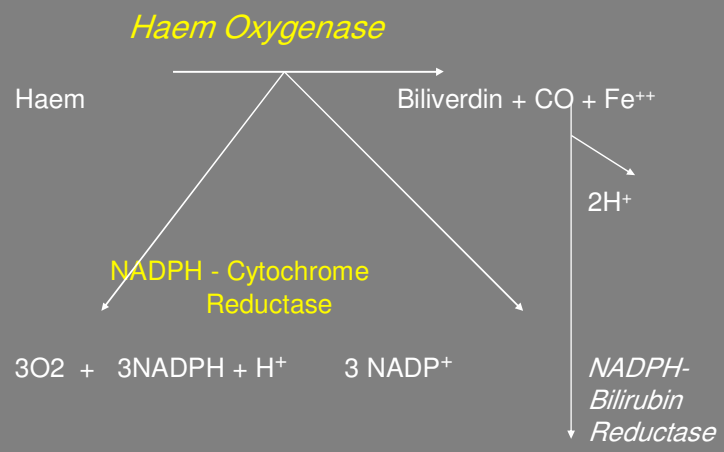
- **Signal for haemolysis:**
  - Loss or alteration of:
    - ✓ Cytoskeleton structure
    - ✓ Active ion pump
    - ✓ Membrane lipids
    - ✓ Membrane glycoproteins
  - Most intracellular components are reutilized.

Fate of Haemoglobin

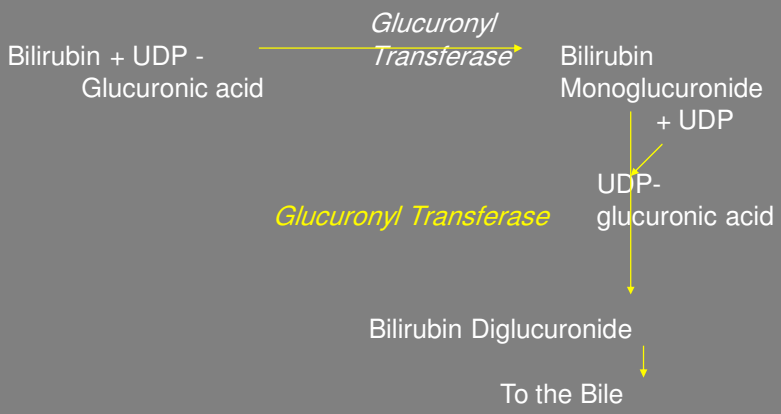




In R.E.S.



In Liver



Daily excretion of Bile Pigments:

- 250-350 ng Bile Pigment excreted in Feces/day
- 1-2 mg Bile Pigment excreted in urine/day

Plasma Level of Bilirubin:

- Total Bilirubin = < 17 µmol/L
- Direct Bilirubin = < 2 µmol/L

Disorder of Bile Pigment Metabolism

Causes:

1. **An increase load of bilirubin arriving at the liver:**
   - due to increased red cell destruction.
   - Absorption of large haematoma.
2. **Defective uptake and transport by the liver cells:**
   - Gilbert's disease.
3. **Disturbance of conjugation:**
   - Liver cell destruction.
   - Reduced glucuronyl transferase activity.
     - ✓ Neonatal jaundice.
     - ✓ Crigler-Najjar Syndrome
     - ✓ Gilbert's disease.
4. **Disturbance of excretion of conjugated bilirubin:**
   - Liver cell destruction.
   - Intra and extrahepatic cholestasis.
   - Dubin-Johnson Syndrome

Jaundice

- Elevation of bile pigments in blood.
- Bile pigments escape into tissues - yellow colouration.
- **Due to:**
  - Production of bile pigments.
  - Failure of liver to conjugate and excrete bile pigments.
  - Decreased excretion of bile pigment due to obstructive of bile duct.

Types of Jaundice :

A. Haemolytic or prehepatic.
B. Hepatic.
C. Obstructive or posthepatic.
D. Congenital non-haemolytic.

Haemolytic Jaundice

- Increase destruction of erythrocytes => ↑Formation of bilirubin
- Elevation of plasma bilirubin.

e.g.
- ✓ In haemolytic anemia
- ✓ Infection
- ✓ G-6-PD deficiency

Hepatic Jaundice

- Caused by liver dysfunction.
- Results from damage to parenchymal cells.
- Decreased conjugation of bilirubin.

e.g.
- ✓ Liver poisons (chloroform phosphorus, CCl 4)
- ✓ Toxins.
- ✓ Hepatitis virus.
- ✓ Engorgement by hepatic vessels in cardiac failure
- ✓ Cirrhoses.

Obstructive Jaundice

- Results from blockage of the hepatic or common bile duct.
- Passage of blood into liver cell is normal.
- Conjugation of bilirubin in liver is normal.
- Failure of conjugated bilirubin to be excreted by bile capillaries.
- Bilirubin reabsorbed by hepatic veins and lymphatics.

Congenital Neonatal Hyperbilirubinaemia

- Decreased Activity of glucuronyl transferase in liver.
- Decreased Conjugation and excretion of bilirubin.
- Increased Unconjugated level in blood.
- Often occurs in neonatal period.
- Treated by phototherapy.

Congenital Hyperbilirubinaemia

- **GILBERT'S DISEASE:**
  - Defective bilirubin transport into liver cells.
  - Occassionally reduced glucuronyl transferase activity.
  - Elevated plasma unconjugated bilirubin (20-35 µmol/L)
  - Harmless.

- **CRIGLER-NAJJAR SYNDROME:**
  - Deficiency in glucuronyl transferase.
  - Significantly elevated plasma unconjugated bilirubin (350 µmol/L)
  - Hyperbilirubinaemia in first few days of life.
  - Kernicterus in newborn.

- **DUBIN-JOHNSONS SYNDROME:**
  - Defective excretion of conjugated bilirubin.
  - Mildly raised conjugated bilirubin.
  - Bilirubin in urine.
  - Harmless.

Types of Bilirubin present in different Jaundice

Defect	Types of Bilirubin
Increased production	**Unconjugated bilirubin**
✓ Haemolytic disease	
Reduced liver uptake of bilirubin	**Unconjugated bilirubin**
✓ Drug competition	
Reduced conjugation of bilirubin	**Unconjugated bilirubin**
✓ Developmental defect	
✓ Drug competition	
✓ Inherited enzyme defects (Gilbert's disease, Criglar Najjar disease)	
Decrease secretion of conjugated bilirubin	**Mainly conjugated bilirubin**
✓ Drug competition	
✓ Inherited defects.	
Obstruction of biliary tree(cholestasis)	**Mainly conjugated bilirubin**
✓ Within the liver (liver cirrhosis, drugs side-effects)	
✓ Outside the liver (gallstone, neoplasm)	

ANAEMIAS

- Anemia is a sign, not a disease
- Anemias are a dynamic process.

- **Definition** : decreased RBC mass and a corresponding decrease in the oxygen-carrying capacity of the blood (Haemoglobins)

- **Working definition** - decreased :
  - Red blood cell count
  - Hemoglobin
  - Hematocrit

Red Blood Cells:

- Red blood cells counts (CBC)
- Hemoglobin (Hgb) –
  - direct measurement (g/dl),
  - method : cyanomethhaemoglobin
- Haematocrit (Hct) -

packed RBC volume (PV) -
method : manual "spun" hematocrit (%)
automated counters calculates Hct
based on RBC number and size (MCV).

Red Blood Cell Indices:

- Mean corpuscular volume (MCV) : average size of the RBCs
  - ✓ MCV= Hct/RBC
- Mean cell haemoglobin (MCH) -
  - ✓ MCH=Hgb/RBC
- Mean cell haemoglobin concentration (MCHC)-
  - ✓ MCHC=Hgb/Hct
- Red blood cell distribution width (RDW) : Index of size variation

Anemia: aetiologies:

- **Production defects**:
    - Nutritional deficiencies-Vitamin B12, folate or iron deficiency.
    - Inflammation/chronic disease.
    - Primary marrow disorders-pure red cell aplasia, myelodysplasia
- **Sequestration -(hypersplenism)-usually associated with mild pancytopenia.**
- **Dilutional-common in hospitalized patients. A patient's plasma volume increases with laying down and when they quit smoking. Possibly responsible for as much as a 3-6% drop in the hematocrit in the first two days of hospitalization.**
- **Blood loss./ Blood destruction-(Haemolytic anemia's).**

Classification of anemias:

- **Anemias can be classified by :-**

1. **Cytometric schemes** -(depending on cell size and hemoglobin-content parameters, such as MCV and MCH),
2. **Erythrokinetic schemes** -(taking into account the rates of RBCs production and destruction)
3. **Biochemical/molecular schemes** -(based on the etiology of the anemia at the molecular level).

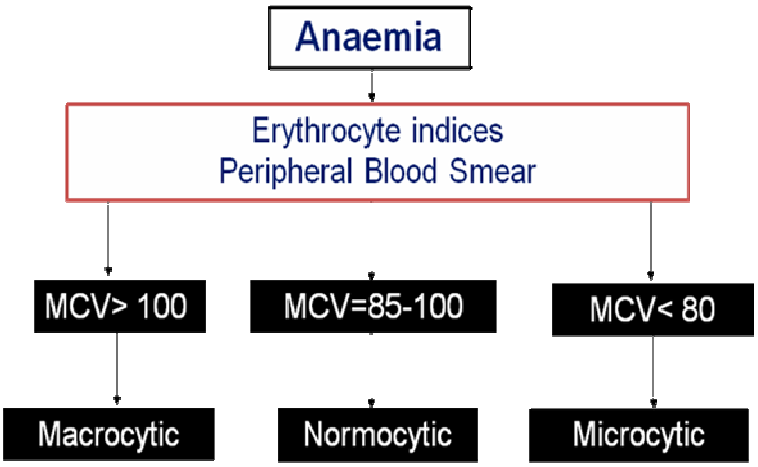
An example: sickle cell anemia

- **Cytometric classification:**
    - ✓ normochromic, normocytic
- **Erythrokinetic classification:**
    - ✓ haemolytic
- **Biochemical/molecular classification:**
    - ✓ DNA point mutation producing amino acid substitution in hemoglobin beta chain (Val. For glu. Acid at position 6 in the beta chain).

Classification of Anaemia

Classified mainly in two ways:

1. According to the morphology of the average red cells.
2. According to the pathophysiologic mechanism of the red cell production.



Classification of Anaemia

1. By Red Cell Morphology:

Initial step in the morphologic classification of anemia

- An anaemic state with altered or normal red cell morphology , i.e. MCV and MCH:
  - MCV: denotes the mean corpuscular volume of red cells (Normal = 85-100 f/l)
  - MCH: denotes mean corpuscular hemoglobin (Normal = 27-32 pg).

Mean Corpuscular Haemoglobin (MCH) :

- MCH expresses the amount of haemoglobin in red blood cell in picogram (pg).

$$MCH = \frac{Hb\ (g/dl\ blood)}{RBC\ Count \times 10^{12}/l}$$

✓ Normal range 27-32 pg

Mean Corpuscular Haemoglobin Concentration (MCHC):

- MCH expresses the amount of haemoglobin in RBC. It is expressed in gm/deciliter.

$$MCHC\ g/dl = \frac{Hb\ (g/dl)}{PCV\ (l/l)}$$

✓ Normal Range 30-35 g/dl

(a) Normocytic Normochromic Anaemia : (MCV = 85-100 fl) (MCH = 30-35 pg)

1. **Acute bleeding.**
2. **Haemolytic anaemia:**

   (a) Extracorpuscular defects immune and non-immune.
   (b) Intracorpuscular defects, membrane,and metabolic defects and hemoglobinopathies.
   (c) Combined defects.
3. **Marrow failure associated with hypoproliferation of hematopoietic cells:**

   (a) Aplastic anaemia.
   (b) Pure red cell aplasia.
   (c) Anaemia of chronic renal failure.
   (d) Anaemia of endocrine disease.
   (e) Toxic depression of bone marrow.

(b) Microcytic - Hypochromic Anaemias : (MCV = < 85 fl) (MCH = < 30 pg)

1. **Iron deficiency.**
2. **Thalassaemias.**
3. **Sideroblastic anaemia:**

   (a) Reflactory.
   (b) Reversible.
   (c) Pyridoxine - responsive.

(c) Macrocytic - Normochromic Anaemias : (MCV = > 100 fl) (MCH = 30-35 pg)

1. **Megaloblastic anaemia:**

   (a) Vit. B12 deficiency.
   (b) folic acid deficiency.
   (c) Others.
2. **Non-Megaloblastic Macrocytic Anaemia.**

2. According to the pathophysiologic mechanism:

A. Increased loss of RBCs

- Acute bleeding

B. Increased destruction of RBCs:

- Haemolytic anaemia

C. Decreased production of RBCs:

1. Marrow failure associated with hypo-proliferation
2. of hematopoietic cells.
3. Marrow failure associated with ineffective
4. erythropoiesis.

Causes of Anaemias:

1. Dyshaemopoietic anaemias : Due to insufficient blood production.
2. Haemolytic anaemias: Due to excessive intra-vascular destruction.
3. Haemorrhagic anaemias : Due to extravascular blood loss.
4. Anaemias of unknown causes.

Dyshaemotopoietic Anaemias

Deficiency of Factors Essential for Erythropoiesis:

1. Iron deficiency.
2. Trace metal (copper) deficiency.
3. Haemopoietic principle deficiency
    a. Extrinsic factor (Vit. B12)
    b. Intrinsic factor (in gastric juice)
4. Other vitamin deficiencies:
    a. Folic acid deficiency.
    b. Pyridoxine deficiency.
    c. Riboflavin deficiency.
    d. Nicotinic acid deficiency.
5. Internal secretion deficiency:
    a. Thyroid hormone deficiency
    b. Pituitary hormone deficiency
6. First class proteins deficiency:
    a. Milk and milk product.
    b. Eggs.
    c. Meat proteins.

Causes of Deficiency in Factors Essential for Erythropoiesis :

- **Food Intake Defect - (Nutritional Anaemias):**
  - Deficiency of:
    1. Proteins
    2. Iron and other metals.
    3. Vitamin C
    4. Vitamin B12
    5. Folic acid

- **Defect of Digestion - due to impaired gastric function:**
  1. Achlorhydria
  2. Deficiency of intrinsic factor
  3. Presence of autoantibodies

- **Defects of absorption and transport:**
  1. Fatty diarrhea, sprue, coeliac disease, diarrhea
  2. Transferrin deficiency, ceruloplasmin deficiency.

- **Defects of storage:**
  - Liver damage.

- **Failure to utilize the factors essential for haemopoiesis:**
  1. Failure of iron utilization.
  2. Sepsis.
  3. Chronic infection (TB, Syphilis)
  4. Nephritis.
  5. Cachexia of malignant disease.
  6. Leukaemia.
  7. Liver cirrhosis.

- **Toxic and aplastic conditions:**
  1. Idiopathic aplastic anaemia.
  2. Damage by Benzol, X-rays, Radium.

Haemolytic Anaemias

Causes:

1. **Infections:**
    - Sepsis and septicaemia:
        i. Streptococcus, Clostridium Welchi (qas gangrene)
        ii. Typhoid fever
        iii. Viral infection

2. **Poisons:**
        i. Chronic lead poisoning
        ii. Acute lead poisoning
        iii. Chemicals (phenylhydrazine, saponins)
        iv. Snake venoms

3. **Allergic haemolytic anaemia:**
    - Pollens or vegetables

Causes:

- **Paroxysmal haemoglobinuria.**
    - ✓ Intravascular haemorrhage due to cold /exertion.
- **Hereditary Intracorpuscular Defects:**
    - ✓ Abnormal haemoglobins (Hb S, Hb C).
    - ✓ Thalassaemias (α and β)
    - ✓ Enzyme deficiency (G-6-PD and PK deficiency)
- **Hereditary abnormalities in corpuscular shape:**
    - ✓ Congenital haemolytic icterus (Hereditary spherocytosis)
    - ✓ Hereditary Elliptocytosis.
- **Hereditary Defects of Unknown cause:**
    - ✓ Familial non-spherocytic haemolytic anaemia
- **Acute haemorrhage:**
    - ✓ Accidents
    - ✓ Surgery
- **Chronic haemorrhage:**
    - ✓ Epistaxis, Menorrhagia
    - ✓ Haemorrhoids
    - ✓ Bleeding duodenal ulcer

- **Haemorrhagic disease:**
  - ✓ Congenital coagulation defects:
    a. Haemophilia (Def. of factor VIII)
    b. Christmas disease (Def. of factor IX)
  - ✓ Acquired coagulation defects:
    a. Vitamin K deficiency
    b. Liver disease
  - ✓ Congenital platelet defects:
    a. Familial thrombocytopenia
  - ✓ Acquired platelet defects:
    a. Irradiation
    b. Drugs (cytotoxic drugs)

Haemolytic Anaemias:

- **Autoimmune haemolytic anemias (AIHA**
- **Microangiopathic haemolytic anemias**
- **Paroxysmal nocturnal haemoglobinuria**
- **Hereditary spherocytosis**
- **Glucose-6-phosphate dehydrogenase deficiency**
- **microspherocytes on PBS , positive direct antibody test (direct Coombs)..**
- **Schistocytes in the peripheral smear**
- **Ham's test (acid-serum lysis), PNH test.Flowcytometry.**
- **Spherocytes , Elevated MCHC,positive osmotic fragility test.**
- **Blister cells, bite cells, Decreased enzyme activity**
- **.(increase retic count may falsely increase G6PD activity**.)..
- qualitative & quntative tests

Anaemias of Unknown Causes

- **Refractory anaemias.**
- **Anaemia secondary to other diseases.**
- **Anaemia due to exertion.**

Iron Deficiency Anemia
Laboratory Findings

- Hypochromic microcytic anemia (↓ RBC count, ↓ MCV)
- ↓ Serum ferritin levels
- ↓ Transferrin saturation (↓ serum Fe, ↑ transferrin)

Pernicious Anaemia
(Addisonial Megaloblastic Anaemia)

- Most common megaloblastic anaemia.
- Due to the absence of intrinsic factor in the gastric juice (atrophy of gastric mucosa).
- Intrinsic factor is needed for absorption of Vit. B12.
- Vit. B12 necessary for Haematopoises.
- ↓Intrinsic factor → ↓Vit. B12 absorption → Ineffective erythropoiesis → Megaloblastic red cells

From here we will discuss plasma proteins

Bio girlz team

Typed by

مجهول

For the student that will downloaded from KSUMS don't forget to

Raed all the file u find it in the folder

Regards ☺

Plasma Proteins

* Normal level:-

- Adult plasma proteins: 6-8 g/dl (recumbent).
  Fluids 6.8-8.5 (ambulatory) due to more water extravasion in the extremities.

* Functions of Proteins:-

1. Oncotic P (Mainly albumin)
2. Nutretive (Mainly albumin) [degredation of albumin] AAJ.
3. Buffering effect.
4. Coagulation and fibrinalysis
5. Defense (functions that depend on Ig, synthesized in the :-
   - Lymphoreticular system
   - The complement system
6. Transport (drugs and hormones)
7. Enzymes and hormones.

* Origins:-

- Albumin, globulin and globulin –formed in the liver.
- Globulin –are formed by plasma cells all over the body in:
  - Bone Marrow
  - Lymph node

* Plasma Proteins:-

a) Biophilic and Suicidal:

- Fibrinogen
- Component of complement
- Ig
- Haptoglobin.

b) Perform transport (carrier)
eg. Albumin, pre-albumin, hormone-binding, Metal binding protein and apo-lipoprotein

- **Transport Function of Plasma Proteins:**

Carrier Protein	Carrier function
Pre-Albumin	- Retinol (Vit A) - T4&T3
Albumin	- Inorganic constituent of plasma(Ca) - Free fatty acid - Hormones (T4&T3) - Excretory product(Unconjugated bilirubin) - Drugs & other toxic substances
Hormone-binding protein	- Corticoids - Sex hormone -Thyroid homones each have their own specific binding proteins
Metal-binding protein	Copper; by ceruloplasmin Iron; by transfering
Apo-Lipoproteins	- Lipids (transport of essential metabolites)

* Change in the total serum proteins:-

- Measuring of total serum proteins is misleading:
  - Hypo-albuminaemia may be balanced by hypergammaglobunaemia.
  - Proteins other than albumin may have large 90 change in cone still not detectable as a change in total serum protein.

Changes → Hyper proteinaemia
Changes → Hypo proteinaemia → Mainly due to hypoalbuminaemia.

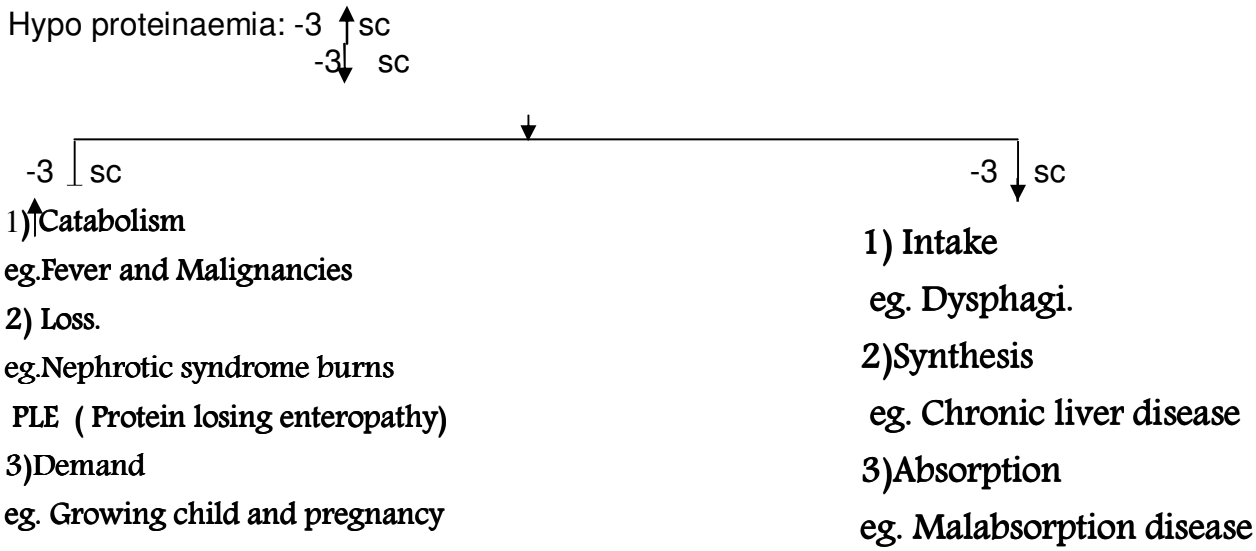
Hyper proteinaemia :- (more than 9 g/dl).

False

- **Dehydration eg. Vomiting, diarrhea or diabetic ketoacidosis**
- **Artificial ↑ Prolonged tornigue application Stasis could se protein and protein bound substance as Ca^{+2} by 10-15%**

True
(due to hyperglobulinemia)

- **Monoclonal (up to 20 g/dl). eg. Multiple myeloma**
- **Polyclonal (up to 14 g/dl) eg.Chronic liver diseases T.B, Sorcidosis, rheumatoid arthritis**



Serum albumin :

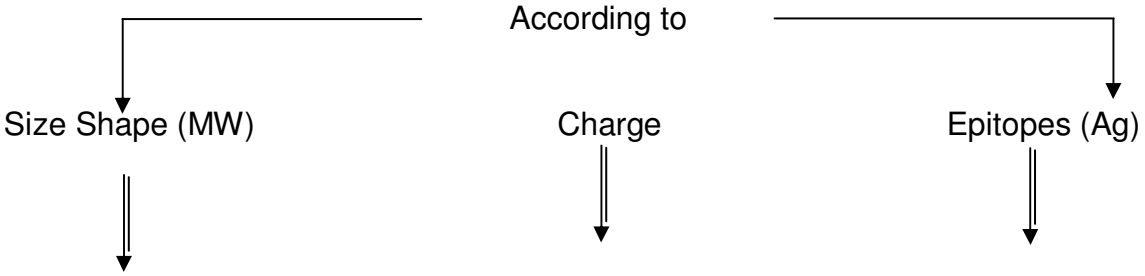
- one of the most protein concentration .
- lost early in nephritic syndrome .
- anything happen in the body will be reflected on albumin .

Fraction of Serum Proteins :-

1. **Chemical Precipitation methods :**
   - By Biuret's methods followed by protein, globulin & in estimation of albumin

2. **Non- specific precipition method :**
   - A number of colloid solutions are stabilized by albumin & are ppt. by globulins especially abnormal globulin this is the principal of the flocculation tests used as liver function test.

3. **Physical method :**



N.B.
Measurment of proteins electrophoresis
Albumin ⟶ Solubelization
Globulin ⟶ Precipitation

(1) RID
(2)Immuno

Ultra Centrifugation :-

- Proteins will separate in to fractions depend on their sedimentation constants which are the property of MW, shape & density of proteins
- At 60,000 rev/min the refractine index of the boundary b/w solvent & the protein is visualized by an optic system
- The results given is Srerrbeg units,
- **Advantage :** Most useful for the determination of MW of protein
- **Disadvantage :** high cost of each analysis & poor resolving capacity

Electrophoresis :-

- It depends on **the charge** carried by protein carries no charge
- **2 types** :
  - **Boundary technique :** Free fluid
  - **Zone electrophoresis** : Stabilizing media, cellulose acetate (Hb), Starch gell, Polyacrylamid gel 'have small pores, best for separation of genetic proteins & isozymes. Fraction total proteins liver

Q- what u prefer to measure (total protein or fraction) ?

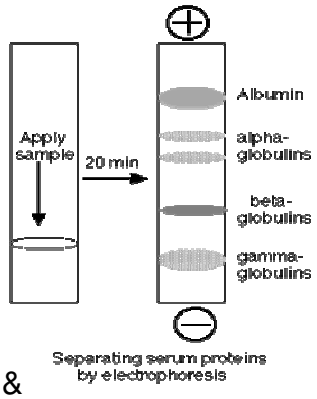
We prefer fraction cuz total protein is misleading .
e.g. liver disease P.t if we measure the total we find it normal but, (A/G ratio changed)
(decrease albumin & increase globulin) So, its apparently normal but actually not .
- also when we measure the percentage change its normal 4 total protein but, actually speaking its changed .

Individual Protein Fractions

- Most plasma proteins are glycoproteins, the amount of CHO varying form 1% (albumin) to 40% (acid glycoprotein also called or somucoid)
- Most plasma protein are synthesized in liver except.
  - Ig by the lymphocytes – Apolipoprotein by Enterocytes.
- Catobolism of plasma proteins is degraded throughout the body after being taken up by cells

❖ **Individual Protein fractions :-**

1) Albumin
2) Globulins : Heterogeneous Gp. + α1 , α2 , β & γ Globulins



✓ **Alpha1 Globulins :-**

1. alpha1 Anti trypsin constitutes about 90% of this fraction "Main"
2. Also include : alpha1 acid glycoprotein, trans cortin, corticosteroid Binding protein, prothrombin, alpha1 fetoprotein & alpha1 lipoprotein : HDL .

1. *alpha1 Anti trypsin (alpha1 protease inhibitor AP_1):*

- Produced by : Hepatocyte & Macrophges.
- Proteases as Trypsin, chymotrypsin, Elastase & Thrombin III continually being released in circulation, AP : inhibits the activity of these proteases.
- In congenital deficiency (homozygous state) patients are prone to pulmonary emphysema, Neonatal hepatitis may proceed to cirrhosis.
- It is increased in acute inflammation & infection cie. It increases in acute phase destruction.

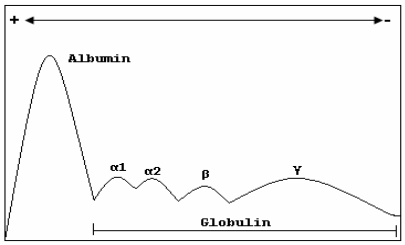
2. *Alpha 1 Fetoprotein (AFP)*

- It is a normal fetal protein, which starts to appear at 6th week. Maximum at 12-15 weeks. It decreases after birth to reach up to 15 mg/l at adult hood.
- It's function is unclear, But it may play an important immunoregulatory role during pregnancy.
- Screening programs during pregnancy involve measurement of AFP in maternal serum where it ↑↑↑ in open neural defects while it ⇓⇓ Down's syndrome.
- AFP detection is very useful in Primary liver cancer
- Other causes of increase include : gonadal teratoma, germ-cell toumor, hepatoma "used as tumor marker"
- Non malignant causes: hepatitis, cirrhosis, & pregnancy. ⟹↑ed AFP.

N.B. Embryonic & Fetal protein associated with human neoplasia :
- Several fetal proteins are synthesized in human tumors : they are released in biological fluid & are useful in diagnosis of malignancy (But not specific) eg.alpha1 fetoprotein &alpha2 ferroprotein.

* *Alpha2 – ferroprotein :-*
  - It's a 17 S iron –containing protein synthesized in liver.
  - Found in fetal organs & serum
  - Increase in Child hood : nephorblastoma, leukemia, hepatoma.
    Adult : Hepatoma, cholngio, carcinoma, lymphoma.

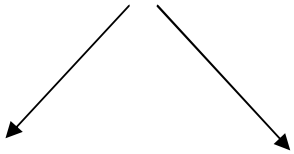
* *Carcino-embryonic antigen :*
  - It is normally up to 2.5 mg/l
  - Elevated levels produced by tumors of ectoderm origins.
  - Elevated levels also occure in smoker & with inflammatory disease of the bowel, lung & chronic liver diseases.



* **Alpha2 Globulin :** this includes ;
  Hepatoglobulin (H_p), alpha$_2$ Macroglobulin, Ceruloplasmin, alpha$_2$ lipoprotein (Pre B : VLDL) which↑ in Pre-B-lipoprotenemia.
  - In alpha2 Globulins : Hepatoglobulin : Carriers Hb "free Hb"
    Ceruloplasmin : Carries metal which is copper.

1. Hepotogolulin (Hp) :

- It's major sythisis occurs in hepoatocytes.
- It binds to free Hb)any to only 2%destruction of RBC /day will completely deplete plasma Hp in the absence of a stimulus for production.
- In case of hepatoglobulin depletion, with further lysis, Hb may be oxidized methemoglobin



Metheme. Globin

- The homoprexin – heme complexes are removed by RES (as in case of Hp- Hb complexes) while albumin (lower affinity).

Mehene ⟶ methemalbumin : releases heme t5o hemopexin directly or go to the lever

N.B : **1) RES . Reticulo-endothelial system** (macrophagis, spleen, Bone marrow)

2) homopexin has high affinity to Hb.

- ↑↑evels of Hp : tissue destruction & malignancy, Recovery stage of burns." b/c of loss of proteins."
- ↑↑Levels of Hp: intravascular hemolysis, ineffective erythropocisis also hepato cellular damage

N.B: 1) Hp. Is an acute phase protein (↑inflammation & infection)

2) In chronic liver disease : (pattern); ↓albumin. Begin between B & gamma ⟸ Polyclonal gammopathy

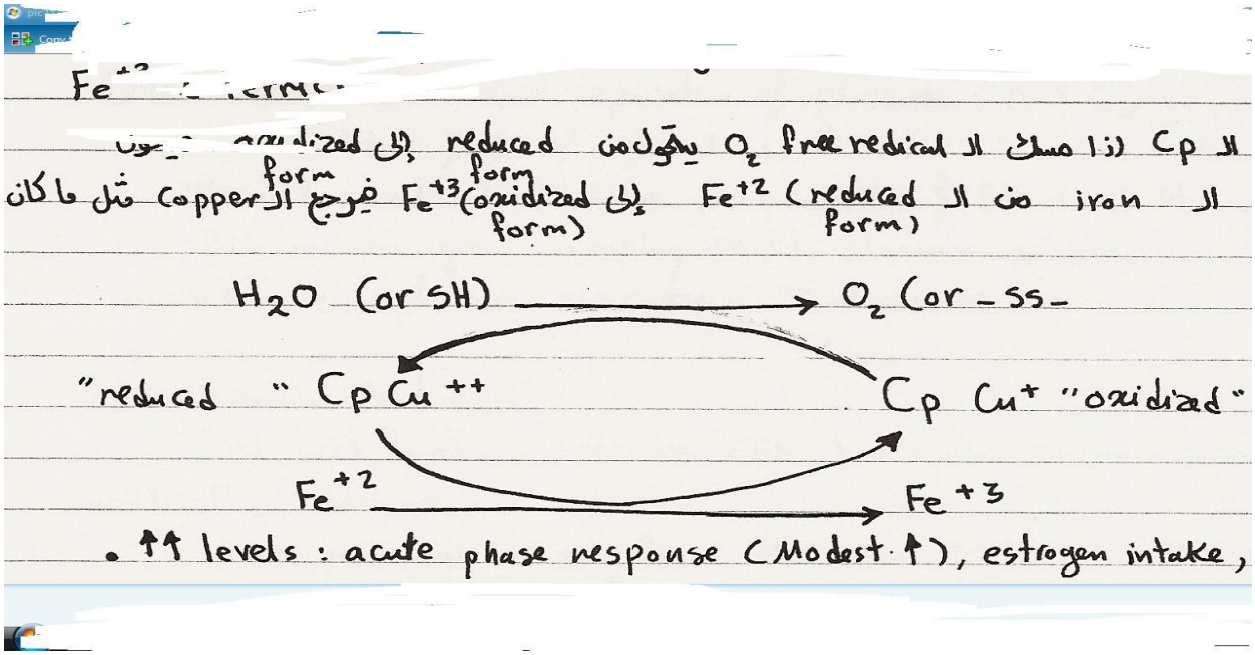
3) **Other polyclonal : TB, arthritis, sarcoidosis.**

2. alpha2 Macroglobulin :

- It is a very large molecule, with a Molecular mass ~ 750 dalton thus doesn't diffuse from plasma to extra cellular fluid.
- It's produced by liver
- Other proteinse inhibitors: alpha1 anti-chymotypsin, anti-thrombin III e 1 estrase inhibitor, Protein C & Plasmonogen activator inhibitor.
- ↑↑ Levels : nephritic syndrome & estrogen intake (↑ synthesis)
- It also binds many cytokines & help their uptake by cells.

N.B : 1- It's retained with the loss of other low MW proteins.
2- Not lost easiy.
3- Pattern of neprotic syndrome;
albumin : ↓ alpha2 globulin : (mainly increas ed alpha2 macroglobulin)
B- globulin: ↑ / gamma - region: ↓

3. **Ceruloplasmin (Cp)** : "Blue in color , b/c of copper"
- It's a copper binding protein that has the ability to "scavenges" O_2 derived free redicals.
- It has the capacity to catalyze oxidation of Fe^{+2} (ferrous) to Fe^{+3} (ferric)



- ↑↑ Levels: acute phase response(modest ↑), estrogen itake, & pregnancy
- ↓↓ Levels : Wilson's desease (hepatolenticular) malabsorption.

N.B. 3 Proteins ↑ed in pregnancy : alpha1 –fetoprotein – Cp – Alkaline phosphatase.

* **B- Glublin** : (↑ed in nephritic syndrome pattern)

❖ If the serum is Fresh two B bands are seen : B_1 & B_2 (C3 complement component)

If the serum is fresh : 2 B bands are gean B_1 & B_2

- It includes : Transafering, hamopexion, C_4 B lipoprotein : LDL fibrinogen, C-reactine protein, some immunoglobulin are B-globulin.
- In nor-fresh (old) sample only 1 Band for B glob lin.
- In B-globulin : hemopexin carries Hb.
  Transferrin carries metal which is iron.

1. **Fibrinogen :-** "important in coagulation + in Plasma Not serum"
   - (300 – 400 mg/dl) or (1-4 g/l) absent in serum.
   - In many inflammatory diseases, rheumatic fever, premonia.
   - In Congeritals as afibrinogenemia, acquired in terminal liver disease, premature separation of placenta (DIC) Placenta will detach from the wall
   - ↑↑ It runs between B & gamma globulins.
   - ↓↓ Transformed in to fibririn in process of blood clotting
   - Fibrinogen gives viscosity to Bl. Plasma helping the maintenance of blood viscosity & pressure.

2. C- reactive protein:-

- First was found in reaction with bacterial pneumococa,then with other antigens.

- It occupies any where from the slow gamma to mid B region
- CRP is some how involved in body in response to foreign material.
- It is considered in immune regulatory function participation.
- Level in MI, stress, trauma, infection inflammation ↑
- Detect early inflammatory reactions, that's why it is 1st protein to in inflammation & 1st one that returns to normal levels!!

β_2 microglobulin :

- In surface of **nucleated cell**
- HLA human lymphocyte antigen
- ↑↑ level in renal failure , inflammation & neoplasm
- It's clinical value in malignant to test renal tubular function , particularly in **Kidney transplant** recipients

Pre-Albumin	Albumin
-Low concentration -T 1/2 : **2** days -Reflex acute deficiency (+ve) -T3&T4 carrier -Liver disease -Bind to **retinol** -Not seen normally BUT it seen by high resolution of electrophoresis	-large 66000 MW -T 1/2 : **20** days - Reflex acute deficiency (- ve) - bilirubin , FFA , Ca++ transport -special for **Liver** - colloid oncotic pressure -A.A > for tissue - chronic deficiency stasis - ↑ : Albuminuria – nephritic – nephritic – dehydration - ↓ : Edema – blood volume - fraction of electrophoresis supporting **cellulose acetate**

- Band of Albumin : Homogeneous - α1 Globulin the band is : Heterogeneous

Immunoglobulin

- They are group of structurally related proteins that function as Anti-bodies.
- They are synthesized by lymphoreticular system.
- Immunoglobulin are made of 4 polypeptidechanis : 2 heavy chains are composed of 5 classes, while the light chains are 2 types

- The heavy chains (5);

⇐ Ig M : are pen tamers found of 5 units, connected through J-protein (acute phase)

- Ig G : Can cross the placenta (chronic inflammation)
- Ig A : present secreted in the alimentary tract is a diner
- Ig E : low fraction, delay hypersensitivity. It's binding site is on basophiles.

- Ig D : as Ig E.

Note: T-cell (lymphocytes) → cell mediated immunity
B-cell (lymphocytes) Humeral immunity

Gamma Globulin:- →

- Agammaglobulinemia : less than 0.1g/dl
- Hypo gammaglobulinemia : 0.1-0.7g/dl

Causes:-

In infants : it's normal to have transient hypo gammaglobulinemia till 6 month (ed infection) after 6 months ⟹ abnormal acquired : nephritic syndrome.

Acute Phase Reaction

(not indicative only to acute reactions but to other diseases)

- These are groups of plasma proteins which show marked ↑ > 50% in concentration. During the early stages of disorders with tissue lesions accompanied by inflammation (trauma, septic necrosis & infection) whether it is acute or chronic.
- There are $+^{ve}$ & $-^{ve}$ acute phase Reactants.

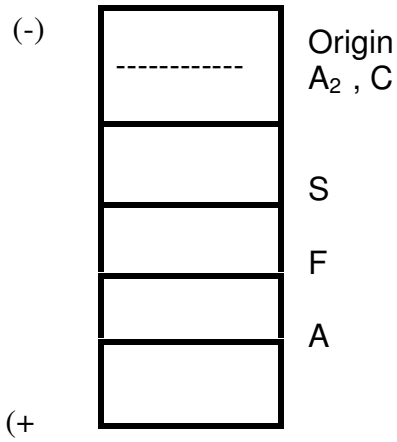
1. eds synthesis & release of other proteins ($+^{ve}$ phase proteins) as:
    1) C-reactive protein
    2) Protease inhibitor (α1 Antitrypsin – α2 macroglobulin – Antithrombin111 – α1 elastase inhibtor)
    3) α1 Glycoprotein
    4) Fibrinogen
    5) Ceruloplasmin
    6) Complement Component ($C_3 + C_n$)
    7) Hepatoglobulin

2. ($-^{ve}$ acute Reactant) : ↓ ed in inflammation;
    1) Prealbumin "also ↓ed in ↓ed nutrition"
    2) Albumin " free albumin"
    3) Transferrin

Methods of Estimation of Hb

1. Electrophoresis.
-at alkaline pH : 8.6
-at acidic pH: 6.0

2. Iso electric focusing
- Separate on the basis of iso electronic pH of Hb variation
-Simple method
-Doesn't separate all variation



-Simple procedure
-Accurate
-Useful for identification of count & variation.
-Can be quantified by Densetometer.

Estimation of Total Hb: → Auto- analyzer
→ Manually (not done now days)

More accurate test.. ⟸ Immunocheminal for separate protein

1. **Immuno diffusion (RID) : Radial Immuno Diffusion**.
    - For specific protein identification.
    - Simple.
    - Proteins are identified on terms of precipitant react respective Anti bodies.

2. **Immunoelectrophoresis :**
    - More sophisticated test.
    - Immune diffusion plus electrical field
    - Rocket immunoelectrophoresis.
    - Quantitative method
    - Accurate but complex
    - Take a long time.

Examples of Organ-Specific Profiles:-

Liver function test : Bilirubin, Alkaline phosphates transaminase,

Albumin.

Note : A/G ratio ↓ in Chronic liver disease

Enzymes of liver:

On biliary canicili
" used in case of Sterisis eg. Stones" .
1) Alkaline phosphates
2) gamma g-t

Inside the cell AST.
ALT
"used when liver cells are affected.
ALT : more liver specific.

* Electrolyte profile : Na^+ , K^+ , CL^- , HCO_3^-
* Acid –base balance ; pH, PCO_2 , HCO_3
* Cardia profile : CPK, CPK MB, LDH, AST.

⟹ in Myocardial infarction :-

- CPK "total " & AST ↑ together & decrease together.+
- LDH last one to ↑ & last one to ↓
- CPK MB ; 1st to ↑ & 1st to ↓
- Troponin are used in MI

Note that CPK MB/ CPK total ration in ❤ more than 30%.

Note:
AST : Aspartate transaminase ; ALT : Allanine transaminase ; A/G : Albumin/Globulin
LDH : lactate dehydrogense ; CPK : Creative phosphokinase ; MB : sub units

* Endo crier profile ; T_3 , T_4 , TSH for thyroxin function
* Muscle function : Mg^{+2} , K^+ ,aldolase
  Note: in skeletal MS. LDH,AST.
  the CPK MB/CPK "total" ration doesn't exceed 5%

* Diabetes Mellitus : Acid-base balance used in diabetic ketoacidosis for diagnosis: fasting g/c.level or GTT(g/c . Tolerance test) for follow up : Hb A_{1c}
* Kidney function : Uric acid, urea, creatinine. Electrolytes (Na^+ , K^+)
* In Rickets :
  - Ca^{++} " ↓ ed"
  - Vit. D
  - PTH "parathyroid hormone = Parathormone"
  - ↑ Phosphate.

* Note : Chronic Renal Failure :-
  - ↓ Ca^{+2}
  - ↑ Phosphate
  - Metabolic Acidosis ⟹ ionized form

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